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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,785	02/06/2004	Eric Finzi	6863-67727	7913

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KLARQUIST SPARKMAN, LLP
121 SW SALMON STREET
SUITE 1600
PORTLAND, OR 97204

EXAMINER

FORD, VANESSA L

ART UNIT	PAPER NUMBER
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1645

MAIL DATE	DELIVERY MODE
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10/01/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/773,785

Applicant(s)

FINZI, ERIC

Examiner

Vanessa L. Ford

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 23, 2007 has been entered. Applicant's submission of Exhibit A, "Online Counseling at eTherapistOnline.com" is acknowledged. Claims 1 and 8 have been amended.

Rejection Withdrawn

2. In view of Applicant's amendment and response the rejection under 35 U.S.C. 103(a), pages 2-9, paragraph 3 has been withdrawn.

Rejections Maintained

3. The rejection of claims 1-15 and 22 under 35 U.S.C. 103(a) is maintained for the reasons set forth on pages 9-14 paragraph 4 of the Final Office Action.

The rejection is reiterated below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1-15 and 22 are rejected under 35 U.S.C. 103(a) as unpatentable over Jahanshahi et al (*Journal of Neurology, Neurosurgery and Psychiatry* (1992, 55:229-231) in view of Binder (*U.S. Patent No. 5,714, 468 published February 3, 1998*) and further in view of Carruthers et al (*U.S. Patent No. 6,358, 917 B1, published March 19, 2002*).

The claims are directed to a method of treating primary depression in subject comprising administering to the subject with primary depression a therapeutically effective amount of a neurotoxin to a facial muscle to cause paralysis of the facial muscle, thereby decreasing the ability of the subject to frown and treating primary depression in the subject.

Jahanshahi et al teach a method of treating patients suffering from depression (e.g. psychological functioning) before and after administration of botulinum toxin (see the Title and the Abstract). Jahanshahi et al teach that depression can result from primary central neurotransmitter dysfunction (page 229). Jahanshahi et al teach that in this study there was a significant improvement in depression of patients that received botulinum toxin injections (page 231). Jahanshahi et al suggest that use of other concepts or techniques may be help with direct management of psychological aspects, body concept and low self-esteem (page 231). Jahanshahi et al that depression may constitute a reaction to the postural abnormality of the head (page 239).

Jahanshahi et al do not teach administering botulinum toxin to a facial muscle such as a frontalis muscle, an orbicularis oculi muscle, procerus muscle, a corrugator supercilli muscle or depressor anguli oris muscle.

Binder teaches that botulinum toxin can be administered to various muscles in the face and head including the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris (see columns 6-7 and figure 1). Binder teaches that headaches may be associated with depression (column 1). Binder teaches that botulinum toxin when administered to patients with headaches is effective in reducing pain and symptoms associated with or the onset of headaches in mammals (see the Abstract). Binder teaches that botulinum toxin can be administered in a dose of up to about 1,000 units although individual dosages of about 15-30 units are preferred (columns 5-6). Binder teaches that botulinum toxin injection be effective up to about 3 to 6 months (column 7). Therefore the combination of prior art references teach the claim limitation "...further comprising administering an additional dose of 30-50 unit equivalents of botulinum A to the facial muscle after about two to six months".

Jahanshahi et al and Binder do not teach claim limitation "... affecting the ability of the subject to frown".

Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth (see the Abstract). Carruthers et al teach that this condition is called "sad mouth" column 2).

It would be *prima facie* obvious at the time the invention was made to administer botulinum toxin to patients suffering from depression as well as affecting the ability of the patient to frown or scowl because Jahanshahi et al teach that administering

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botulinum toxin to torticollis patients experiencing depression significantly reduced levels of depression and anxiety, Binder teaches that botulinum toxin can be effectively administered to facial muscles such as the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris and Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin to the facial muscles of patients suffering from depression would be an effective way to treat depression as well as anxiety in these patients.

Applicant's Arguments

- A) Applicant urges that the combination of Jahanshahi et al, Binder or Carruthers et al do not teach, suggest or render obvious the treatment of major depression.
- B) Applicant urges that they have submitted evidence of the unexpectedly superior results obtained using the claimed methods. Applicant urges that the documentation of the unexpected superior results obtained using the claimed methods overcome any prima facie case of obviousness that could be made over the impermissible combination Murray et al, Binder and Carruthers et al.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed July 23, 2007 have been fully considered but they are not persuasive. It should be noted that this rejection is set forth as Jahanshahi et al in view of Binder and further in view of Carruthers et al and not Murray et al in view of Binder and further in view of Carruthers et al.

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A) In response to applicant's argument that no case of *prima facie* obviousness was established the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, one of ordinary skill would be motivated to use botulinum toxin to administer botulinum toxin to patients suffering from depression as well as affecting the ability of the patient to frown or scowl because Jahanshahi et al teach a method of treating patients suffering from depression (e.g. psychological functioning) before and after administration of botulinum toxin, Binder teaches that botulinum toxin can be effectively administered to facial muscles such as the frontalis, orbicularis oculi, procerus muscle, a corrugator supercilli and depressor anguli oris and Carruthers et al teach that botulinum toxin can be used to cause paralysis to a depressor anguli oris in a patient to alleviate downturn at the corners of a patient's mouth.

B) To address Applicant's unexpected superior evidence, (e.g. Exhibit A, Finzi et al), while it is true that Finzi et al has established that botulinum toxin treats major depression, however, there is nothing on the record that suggest that the combination of references does not teach a method treating depression by administering to facial muscles of a patient botulinum toxin.

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In view of all of the above, this rejection is maintained.

4. The rejection under 35 U.S.C. 103(a) is maintained for claims 16-21 for the reasons set forth on pages 14-19, paragraph 5 of the Final Office Action.

The rejection is reiterated below:

The rejection was on the grounds that the teaching of Jahanshahi et al, Binder and Carruthers et al as applied to claims 1-5 and 22 above and further in view of Wagstaff et al.

Jahanshahi et al, Binder and Carruthers et al have been described previously.

Jahanshahi et al, Binder and Carruthers et al do not teach an additional modality of treatment for depression.

Wagstaff et al teach that paroxetine is a selective serotonin reuptake inhibitor (SSRI) with antidepressant and anxiolytic activity (see the Abstract). Wagstaff et al teach that paroxetine is effective at treating depressive disorder (see the Abstract). Wagstaff et al teach that the common adverse effects with using paroxetine include headache (see the Abstract). Wagstaff et al teach that paroxetine is an important first-line option for treatment of major depressive disorder, obsessive-compulsive disorder, panic disorder, social anxiety disorder, general anxiety disorder and post-traumatic stress disorder (see the Abstract).

It would be *prima facie* obvious at the time the invention was made to use an additional modality of treatment for depression such as administration of SSRIs to patients suffering from depression because Jahanshahi et al suggest that use of other concepts may be helpful with direct management of psychological aspects such as body concept and low self-esteem. One of ordinary skill in the art would be motivated to administer SSRIs to treat patients with torticollis who suffer from depression because Jahanshahi et al has demonstrated that these patients experience psychological aspects such as body concept and low self-esteem even after botulinum toxin treatment. Therefore, one of skill in the art would reasonably conclude that the addition of a SSRI such as paroxetine would be effective at treating these patients since Wagstaff et al teach that paroxetine is effective in treating depressive disorders such as social anxiety disorder and general anxiety disorder. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin and a SSRI to patients suffering from depression would be effective in treating depression.

Applicant's Arguments

- A) Applicant urges that Binder does not teach, suggest or render obvious the treatment of major depression. Applicant urges that Binder does not teach, suggest or render obvious the introduction of botulinum toxin into a facial muscle that affects the ability of a subject to scowl or frown
- B) Applicant urges that they have submitted evidence of unexpectedly superior results obtained using the claimed method specifically documenting the superior results with injection of botulinum toxin and additional treatment modalities even when PAXIL or ZOLOFT have failed. Applicant urges that the documentation of the unexpected superior results obtained using the claimed methods overcome any *prima facie* case of obviousness that could be made over the impermissible combination Murray et al, Binder and Caruthers et al.

Examiner's Response to Applicant's Arguments

- A) In response to applicant's argument that no case of *prima facie* obviousness was established the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir.

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1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, one of ordinary skill would be motivated to use botulinum toxin to administer SSRIs to treat patients who suffer from depression because Jahanshahi et al has demonstrated that these patients experience psychological aspects such as body concept and low self-esteem even after botulinum toxin treatment. Therefore, one of skill in the art would reasonably conclude that the addition of a SSRI such as paroxetine would be effective at treating these patients since Wagstaff et al teach that paroxetine is effective in treating depressive disorders such as social anxiety disorder and general anxiety disorder. Based on the teachings of the combined prior art references, it would be expected barring evidence to the contrary, that the administration of botulinum toxin and a SSRI to patients suffering from depression would be effective in treating depression.

B) Although Applicant has presented unexpected superior evidence showing that botulinum toxin in addition to SSRIs are effective in treating depression, there is nothing on the record that suggest that the combination of references does not teach a method treating depression by administering to facial muscles of a patient botulinum toxin and a selective serotonin reuptake inhibitor. It should be noted that the administration of botulinum toxin treats depression as well as the headaches that may be caused by administration of the serotonin reuptake inhibitor which is another reason one of skill in the art would be motivated to combine the administration of botulinum toxin with SSRI therapy.

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In view of all of the above, this rejection is maintained.

New Grounds of Objection/Rejection

5. Claim 22 is objected to for the following informality: Claim 22 recites (Previously Presented). This should be changed to (Currently Amended) since Applicant has amended the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 22 is rejected under 35 U.S.C. 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claim 22 recites "primary major depression". It is unclear as to what Applicant intends by this phrase. Clarification/correction is required.

Status of Claims

7. No claims allowed.

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Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Vanessa L. Ford
Biotechnology Patent Examiner
September 24, 2007



NITA MINNIFIELD
PRIMARY EXAMINER
9-24-07